Biochemistry 3300 Problems (and Solutions) Metabolism III

(1) What is the role of fermentation in aerobic organisms?

(2) How does TPP facilitate a-keto acid decarboxylation?

(3) Which dietary sugars (starch, maltose, lactose, sucrose) require hexokinase for entry into glycolysis?

(4) Identify each of the oxidation-reduction reactions catalyzed by the pyruvate dehydrogenase complex.

(5) Arsenite is an inhibitor of some enzymes *in vitro*. What is the mechanism of arsenite inhibition?

(6) Consider the catabolism of glucose in yeast under aerobic conditions. Which enzymes catalyze decarboxylation reactions? What about under anaerobic conditions?

(7) Which enzymes of the TCA cycle utilize a 'covalent' enzyme intermediate?

(8) Identify the irreversible reactions of the TCA cycle. Why are these reactions of particular interest?

(9) What is coordinated regulation and when is it utilized in metabolism?

(10) Provide an overall reaction for the conversion of:

a) glucose to succinate
b) pyruvate to CO_2
c) galactose to acetyl-CoA

Answers

1- In the absence of oxygen (terminal electron acceptor of respiration), the electron transfer chain and the TCA cycle will stop functioning as NADH (and $FADH_2$) accumulates. Fermentation regenerates NAD^+ from NADH allowing glycolysis to continue to function in the absence of oxygen.

2- TPP form a 'stabilized' carbanion (ylid form) within the thiazolium ring that attacks the α-keto carbon. The thiazolium ring acts as an 'electron sink' that leads to decarboxylation and resonance stabilization of the resulting carbanion / enol. Protonation leads to product release or transfer to a suitable acceptor.

3- Each of the indicated dietary sugars require hexokinase for entry into glycolysis. Only galactose and fructose (in the liver) have routes into glycolysis that do not require hexokinase.

4- E1: α-keto decarboxylation of pyruvate to hydroxyethylthiamine AND hydroxyethylthiamine transfer to oxidized lipoyllysine.
E3: oxidation of reduced lipoyllysine by FAD AND oxidation of $FADH_2$ by NAD^+

5- Arsenite forms irreversible bidentate adducts with vicinyl sulfhydryls. Enzymes that utilize vicintyl disulfides in their reaction mechanism are inhibited.

6- <u>aerobic</u>

Pyruvate dehydrogenase complex	(pyruvate → acetyl-CoA + CO_2)
Isocitrate dehydrogenase	(isocitrate → α-ketoglutarate + CO_2)
α-ketoglutarate dehydrogenase complex	(α-ketoglutarate → succinyl-CoA + CO_2)
<u>anaerobic</u>	
Pyruvate carboxylase	(pyruvate → acetaldehyde + CO_2)

7- α-ketoglutarate dehydrogenase complex
succinyl-CoA synthetase

8- Acetyl-CoA + oxaloacetate → citrate (Citrate synthase)
α-ketoglutarate → succinyl-CoA (α-ketoglutarate dehydrogenase complex)
and arguably Isocitrate → α-ketoglutarate (isocitrate dehydrogenase)
These are the reactions that regulate flux through the TCA cycle.

9- Coordinated regulation involves pathways that share a common metabolic intermediate. In these cases regulatory mechanism activate one pathway at the same time the alternate pathway is inhibited.

10 – a) glucose + 2ADP + 2GDP + $8NAD^+$ → succinate +2ATP +2GTP +8NADH +$8H^+$ + $6CO_2$
(2ATP + 2NADH from glycolysis; 2NADH + $2CO_2$; 2GTP + 4NADH + $4CO_2$ from TCA)
b) pyruvate +1GDP +$4NAD^+$ +1GDP +1FAD → $3CO_2$ +4NADH +$4H^+$ +$1FADH_2$ +1GTP
c) galactose +2ADP +$4NAD^+$ → 2acetyl-CoA +2ATP +$2CO_2$ +4NADH +$4H^+$